

## Abstract

# Fruit and Vegetable Intake and Cardiovascular Disease in the UK Biobank: The Role of Confounding<sup>†</sup>

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**Abstract:** Objectives: Fruit and vegetable (FV) consumption has been inversely associated with cardiovascular disease, but questions remain about the extent to which these results are due to confounding. Methods: From 2006–2010, >0.5 million adults aged 40–69 were recruited to the UK Biobank. Participants free from ischaemic heart disease (IHD) or stroke, with complete information on key covariates, were analysed (n = 452,760). Usual FV intakes were measured by frequency questionnaire, categorised into four groups, and calibrated with a 24-h dietary assessment. Multi-variable Cox regression was used to estimate the associations of fruit and/or vegetable intake with IHD, ischaemic stroke, and haemorrhagic stroke, adjusted for socioeconomic status, lifestyle factors, dietary factors, and body mass index. Sequential change in likelihood ratio (LR)  $\chi^2$  was used to quantify the contribution of covariates to model fit. Results: During 12–16 years of follow-up, there were 15,746 IHD events, 5940 ischaemic strokes, and 2154 haemorrhagic strokes. Associations were mostly non-linear. The lowest IHD risk was with the third category of fruit intake (median 216 g/day, HR 0.93 (95% confidence interval 0.90 to 0.97)) and second category of vegetable intake (158 g, 0.95 (0.93, 0.98)). Only the third category of fruit intake and combined FV intake were associated with a lower ischaemic stroke risk (216 g, 0.93 (0.88, 0.99) and 375 g, 0.92 (0.86, 0.97) respectively). Only the highest category of fruit intake (293 g, 0.87 (0.78, 0.98)) and second category of vegetable intake (158 g, 0.89 (0.83, 0.96)) were associated with a lower haemorrhagic stroke risk. Full adjustment reduced the LR  $\chi^2$  of associations with ischaemic disease by 87–92% and haemorrhagic stroke by 66–70%. For IHD and ischaemic stroke, the biggest reductions were with the addition of lifestyle factors in models of FV or fruit intake and socioeconomic status for vegetable intake. Discussion: The relationship between fruit and/or vegetable intake and these cardiovascular outcomes is heavily confounded by socioeconomic, lifestyle, and dietary factors. Residual confounding may explain more of the remaining association. Therefore, caution should be exercised when estimating the burden of disease attributable to low fruit and vegetable intake.

**Keywords:** fruit; vegetable; cardiovascular disease; UK Biobank; confounding; prospective cohort



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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The UK Biobank is an open access resource. The data underlying this project were accessed using application number 67506.

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